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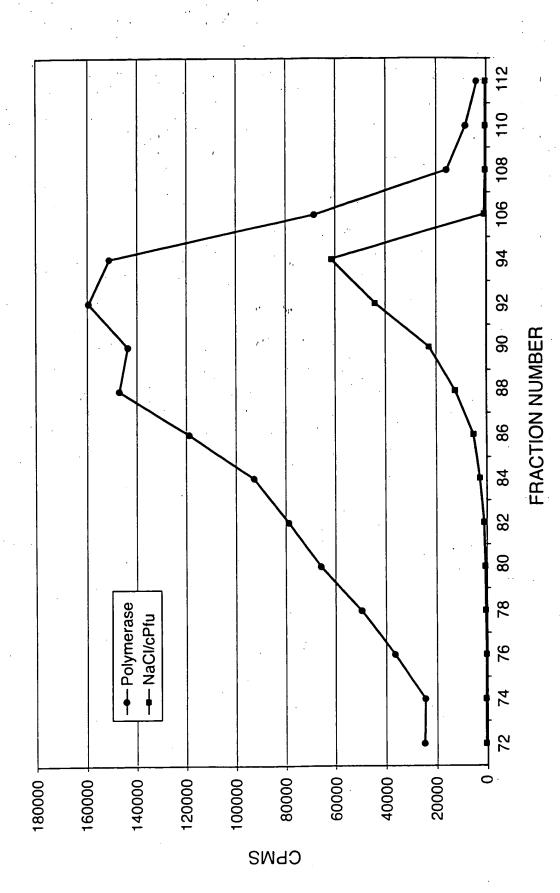
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Title: Pfu REPLICATION ACCESSORY FACTORS AND METHODS OF USE
Inventors: Holly H. Hogrefe et al.
Application No.: Not Yet Assigned
Filed: April 20, 2004
Attorney Docket No.: 04121.0161-02000
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Title: Pfu REPLICATION ACCESSORY FACTORS AND METHODS OF USE Inventors: Holly H. Hogrefe et al. Application No.: Not Yet Assigned Filed: April 20, 2004 Attorney Docket No.: 04121.0161-02000 Page 2 of 37 (Figure 2) 2/37 CPMS (PCNA) 1000 1200 1600 1400 200 800 9 400 A>>250 B>250 C<250 D<250,>98 E>98 F64-98 G50-64 H36-50 J30-36 K16-30 PROTEIN MOLECULAR WEIGHT OF GEL SLICE

20000

2000

1800

--- PCNA (salt + Pfu)

250000 -

-- Pfu (no salt)

200000

150000

100000

CPMS (Pfu)

USE

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# FIG. 3

### FIG. 4

MPFEIVFEGAKEFAQLIDTASKLIDEAAFKVTEDGISMRAMDPSRVVLID LNLPSSIFSKYEVVEPETIGVNMDHLKKILKRGKAKDTLILKKGEENFLE ITIQGTATRTFRVPLIDVEEMEVDLPELPFTAKVVVLGEVLKDAVKDASL VSDSIKFIARENEFIMKAEGETQEVEIKLTLEDEGLLDIEVQEETKSAYG VSYLSDMVKGLGKADEVTIKFGNEMPMQMEYYIRDEGRLTFLLAPRVEE\*

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#### CLAMP INCREASES PROCESSIVITY OF Pfu

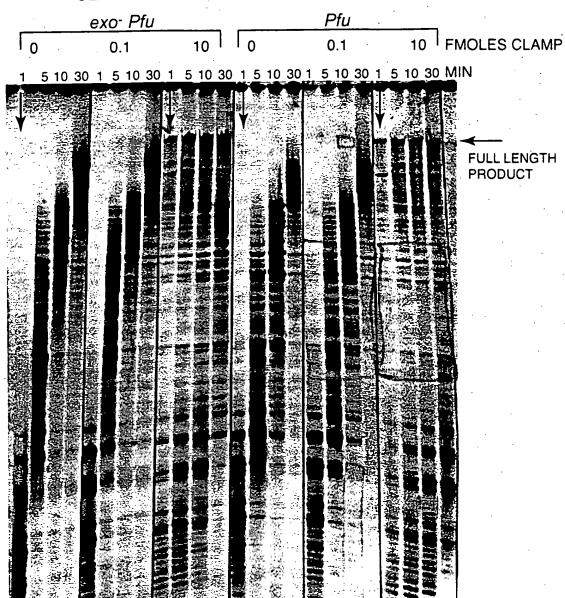


FIG. 5

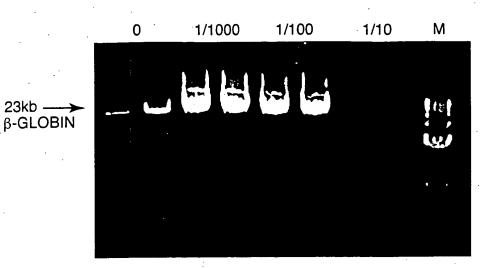
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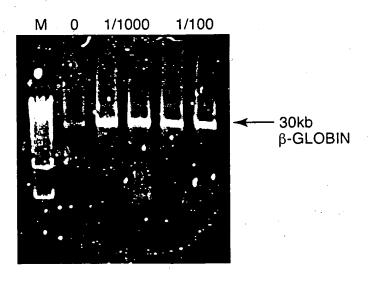
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 $5U \text{ TPL} + 1\mu\text{I OF CLAMP DILUTION} / 50\mu\text{I PCR}$ 

FIG. 6



 $5U \text{ TPL} + 1\mu\text{I OF CLAMP DILUTION} / 50\mu\text{I PCR}$ 

FIG. 7

USE

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# FIG. 8

ACCCAAAATTGTTATTCAGNTCAACGGAGAAGACGGAGTAGANTTGGAAGG AGCTTATCCAGAGAAATGTTCTTAGAGAAGTTACTCTCAGCTCTCAGCTGA TCTANNGTTTTTCCTTCTTTTCTTCTGTTCAGTTATNGCCTAGGATAAGCT TAATAATACTTTGATACCTTTCTTAGTTTAGGTGTGTGAGAGTATGAGCGA AGAGATTAGAGAAGTTAAGGTTCTAGAAAAACCCTGGGTTGAGAAGTATAG ACCTCAAAGACTTGACGACATTGTAGGACAAGAGCACATAGTGAAAAGGCT CAAGCACTACGTCAAAACTGGATCAATGCCCCACCTACTCTTCGCAGGCCC CCCTGGTGTCGGAAAGTGTCTTACTGGAGATACCAAAGTTATAGCTAATGG CCAACTCTTTGAACTTGGAGAACTTGTTGAAAAGCTTTCTGGGGGGAGATT TGGACCAACTCCAGTTAAAGGGCTCAAAGTTCTTGGAATAGATGAGGATGG AAAGCTTAGAGAGTTTGAAGTCCAATACGTCTACAAAGATAGAACTGATAG GTTGATAAAGATAAAACTCAGCTTGGCAGGGAGCTTAAAGTAACTCCGTA TCACCCACTTCTAGTGATTGGAGAGAATGGCGAATTAAAGTGGATTAAGGC TGAAGAACTCAAACTTGGCGACAAGCTTGCAATACCGAGCTTTCTCCCACT TATAACTGGAGAAAATCCCCTTGCAGAGTGGCTTGGTTACTTTATGGGAAG TGGCTATGCTTATCCCAAGAATTCTGTCATCACGTTCACTAACGAAGATCC **ACTCATAAGACAACGCTTTATGGAACTAACAGAGAAACTTTTCCCTGATGC** AAAGATAAGGGAAAGAATTCACGCTGATGGAACTCCAGAAGTTTATGTGGT ATCTAGGAAAGCTTGGAGCCTTGTAAACTCTATTAGCTTAACATTAATACC CAGGGAGGGTGGAAAGGAATTCGTTCTTTCCTTAGGGCATATTCCGACTG CAATGGTCGGATTGAAAGTGATGCAATAGTTTTATCAACCGATAACAATGA TATGGCCCAGCAGATAGCCTATGCTTTAGCCAGCTTTGGAATAATAGCTAA AATGGATGGAGAAGATGTTATTATCTCAGGCTCGGACAACATAGAGAGGTT CCTAAATGAGATTGGCTTTAGCACCCAAAGCAAACTTAAAGAAGCCCAGAA GCTCATTAGAAAAACCAATGTAAGATCCGATGGACTAAAGATTAACTATGA GCTAATCTCCTATGTAAAAGACAGGCTTAGGTTAAATGTCAATGATAAAAG **AAATTTGAGCTACAGAAATGCAAAGGAGCTTTCTTGGGAACTCATGAAAGA** AATTTATTATCGCCTTGAGGAACTGGAGAGACTAAAGAAGGTCTTATCAGA ACCCATCTTGATCGACTGGAATGAAGTAGCAAAGAAGAGTGATGAAGTAAT AGAAAAAGCTAAAATTAGAGCAGAGAAGCTCCTAGAATACATAAAAAGGAGA GAGAAAGCCAAGTTTCAAGGAGTACATTGAGATAGCAAAAGTCCTTGGAAT TAACGTTGAACGTACCATCGAAGCTATGAAGATCTTTGCAAAGAGATACTC AAGCTATGCCGAGATTGGAAGAAAACTTGGAACTTGGAATTTCAATGTAAA AACAATTCTTGAGAGCGACACAGTGGATAACGTTGAAATCCTTGAAAAGAT AAGGAAAATTGAGCTTGAGCTCATAGAGGAAATTCTTTCGGATGGAAAGCT CAAAGAAGGTATAGCATATCTCATTTTCCTCTTCCAGAATGAGCTTTACTG GGACGAGATAACTGAAGTAAAAGAGCTTAGGGGGAGACTTTATAATCTATGA TCTTCATGTTCCTGGCTACCACAACTTTATTGCTGGGAACATGCCAACAGT AGTCCATAACACTACAGCGGCTTTGGCCCCTTGCAAGAGAGCTTTTCGGCGA AAACTGGAGGCATAACTTCCTCGAGTTGAATGCTTCAGATGAAAGAGGTAT AAACGTAATTAGAGAGAAAGTTAAGGAGTTTGCGAGAACAAAGCCTATAGG AGGAGCAAGCTTCAAGATAATTTTCCTTGATGAGGCCGACGCTTTAACTCA AGATGCCCAACAAGCCTTAAGAAGAACCATGGAAATGTTCTCGAGTAACGT TCGCTTTATCTTGAGCTGTAACTACTCCTCCAAGATAATTGAACCCATACA GTCTAGATGTGCAATATTCCGCTTCAGACCTCTCCGCGATGAGGATATAGC GAAGAGACTAAGGTACATTGCCGAAAATGAGGGCTTAGAGCTAACTGAAGA AGGTCTCCAAGCAATACTTTACATAGCAGAAGGAGATATGAGAAGAGCAAT AAACATTCTGCAAGCTGCAGCAGCTCTAGACAAGAAGATCACCGACGAAAA (cont.)

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# FIG. 8 (cont.)

CGTATTCATGGTAGCGAGTAGAGCTAGACCTGAAGATATAAGAGAGATGAT GCTTCTTGCTCTCAAAGGCAACTTCTTGAAGGCCAGAGAAAAGCTTAGGGA GATACTTCTCAAGCAAGGACTTAGTGGAGAAGATGTACTAGTTCAGATGCA TGATAAGATAGGAGAGTATAACTTCAGACTCGTTGAAGGGGCTAATGAAAT AATTCAGCTTGAAGCACTCTTAGCACAGTTCACCCTAATTGGGAAGAAGTG ATGAAGTATGCCAGAGCTTCCCTGGGTAGAAAAATACAGGCCAAAAAAGTT AAGTGAAATTGTAAACCAAGAAGAGGCTATAGAGAAAGTTAGAGCGTGGAT AGAGAGCTGGTTGCATGGCCACCCCCTAAGAAAAAGCCCTATTATTAGC AGGACCCCCAGGGAGCGGAAAGACAACCACAGTCTACGCTCTAGCAAATGA GTACAACTTTGAAGTCATTGAGCTCAACGCGAGTGATGAGAGAACTTATGA AAAAATCTCCAGGTATGTTCAAGCAGCATACACTATGGATATCCTCGGAAA GAGGAGGAAGATAATCTTCCTCGATGAAGCAGATAATATAGAGCCCAGCGG AGCTAAGGAAATCGCAAAACTAATTGATAAGGCCAAAAATCCAATAATAAT GGCTGCAAATAAGTACTGGGAAGTTCCAAAAGAGATCCGAGAAAAAGCTGA AAGGATCCTAAAGAGGGAAGGTATAACAGTTCCAAAAGAAATCCTCCTAGA **AATAGCAAAAAGATCTAGTGGAGATCTAAGAGCAGCTATAAATGATCTACA** GACCGTTGTAGTGGGTGGTTACGAAGATGCTACGCAAGTTTTGGCATATAG AGATGTAGAAAAGACAGTCTTTCAAGCCCTAGGACTCGTCTTTGGAAGTGA CAACGCCAAGAGGGCAAAGATGGCAATGTGGAACTTGGACATGTCCCCTGA TGAATTCCTGCTATGGGTAGATGAGAACATTCCTCACCTCTACCTAAATCC AGAGGAGATTGCCCAGGCGTATGATGCAATTAGTAGAGCCGACATATACCT CGGAAGGGCCGCCAGAACTGGAAACTATTCACTCTGGAAGTACGCAATAGA TATGATGACTGCAGGAGTTGCCGTGGCAGGAGAAAGAGAAGGGGGATTTGT CAAGTTTTATCCTCCCAACACCCTAAAGATTTTAGCGGAAAGCAAAGAAGA **AAGAGAGATCAGAGAGTCCATAATTAAAAAGATAATACGAGAGATGCNCAT** GAGTAGGCTACAGGCAATAGAAACGATGAAAATAATTAGAGAGATTTTCGA AAAAGAAGTTGAGTTTCTAGCTGGAAAGGAAAAAGCTGGTACCATTTGGGG CAAAGCCTTAGCATTAAGAAGGAAACTTAAGGAGCTTGGAATAAGAGAGGA GGAGAAGCCTAAAGTTGAAATTGAAGAAGAGGAAGAAGAAGAAGAAAAAGAC CGAAGAAGAAAAGAGGAAATAGAAGAAAAACCCGAAGAAGAAGAAGAAGA GGAGAAGAAAGAAAAGGAAAAGCcaaAGAAAGGCAAACAAGCAACTCTCTT TGACTTTCTTAAAAAGTGATTACCCTTTTTCTTCTATTAGAGCTCCGAATA AAGTTGGCCCTCTAATTTTTTCTATTGTCTCCTCCACATTAATCTTTACGA ATTGGAATTCCTGCAGCCCGGGGGATCCACTAGTTCTAGAGCGGCCGCCAC CGCGGTGGAGCTCCAGCTTTTGTTCCCTTTAGTGAGGGTTAATTTCGAGCT TGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCA CAATTCCACACAACATACGAACCCGGAAGCATAAATTGTAAACCCNGGGGT GCCTAATGANTGANCTAACTCACATTAATTGCNTTGCGCTCACTGCCCGCT TTCCANTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACNC GCGGGGANAAGCGGTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCATGA CTCGCTGCGCTCGGTCNTCGGCTGCGGCGAACGGTATCAGCTCATCAAAGG CGGTAATACGGTTATCCNCAAATCAGGGGATAACGCAGGAAAAAACTTTNN ACAAAAGGCNNCAAAAGGCGGAAACTAAAAGGCGCNTTCTGGGTTTTTCNT AGGCCCNCCCGANAACTCNAAAAATCAACNCATTCAAGTGGGAAACCAAA GAA

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# FIG. 9

PKIVIQXNGEDGVXLEGAYPEKCS\*RSYSQLSADLXFFLLFFCSVXA\*DK LNNTLIPFLV\*VCES(MSEEIREVKVLEKPWVEKYRPQRLDDIVGQEHIV KRLKHYVKTGSMPHLLFAGPPGVGK [ CLTGDTKVIANGQLFELGELVEKL SGGRFGPTPVKGLKVLGIDEDGKLREFEVQYVYKDRTDRLIKIKTQLGRE LKVTPYHPLLVIGENGELKWIKAEELKLGDKLAIPSFLPLITGENPLAEW LGYFMGSGYAYPKNSVITFTNEDPLIRQRFMELTEKLFPDAKIRERIHAD GTPEVYVVSRKAWSLVNSISLTLIPREGWKGIRSFLRAYSDCNGRIESDA IVLSTDNNDMAQQIAYALASFGIIAKMDGEDVIISGSDNIERFLNEIGFS TQSKLKEAQKLIRKTNVRSDGLKINYELISYVKDRLRLNVNDKRNLSYRN AKELSWELMKEIYYRLEELERLKKVLSEPILIDWNEVAKKSDEVIEKAKI RAEKLLEYIKGERKPSFKEYIEIAKVLGINVERTIEAMKIFAKRYSSYAE IGRKLGTWNFNVKTILESDTVDNVEILEKIRKIELELIEEILSDGKLKEG **IAYLIFLFQNELYWDEITEVKELRGDFIIYDLHVPGYHNFIAGNMPTVVH** NITTAALALARELFGENWRHNFLELNASDERGINVIREKVKEFARTKPIG GASFKIIFLDEADALTQDAQQALRRTMEMFSSNVRFILSCNYSSKIIEPI OSRCAIFRFRPLRDEDIAKRLRYIAENEGLELTEEGLQAILYIAEGDMRR AINILOAAAALDKKITDENVFMVASRARPEDIREMMLLALKGNFLKAREK LREILLKQGLSGEDVLVQMHKEVFNLPIEEPKKVLLADKIGEYNFRLVEG ANEIIQLEALLAQFTLIGKK) \*\*S(MPELPWVEKYRPKKLSEIVNQEEAI EKVRAWIESWLHGHPPKKKALLLAGPPGSGKTTTVYALANEYNFEVIELN ASDERTYEKISRYVQAAYTMDILGKRRKIIFLDEADNIEPSGAKEIAKLI DKAKNPIIMAANKYWEVPKEIREKAELVEYKRLTQRDVMNALIRILKREG ITVPKEILLEIAKRSSGDLRAAINDLQTVVVGGYEDATQVLAYRDVEKTV FQALGLVFGSDNAKRAKMAMWNLDMSPDEFLLWVDENIPHLYLNPEEIAO AYDAISRADIYLGRAARTGNYSLWKYAIDMMTAGVAVAGRKRRGFVKFYP PNTLKILAESKEEREIRESIIKKIIREMXMSRLQAIETMKIIREIFENNL DLAAHFTVFLGLSEKEVEFLAGKEKAGTIWGKALALRRKLKELGIREEEK PKVEIEEEEEEEKTEEEKEEIEEKPEEEKEEEKKEKEKPKKGKQATLFD FLKK) \*LPFFFY\*SSE\*SWPSNFFYCLLHINLYELEFLQPGGSTSSRAAA TAVELQLLFPLVRVNFELGVIMVIAVSCVKLLSAHNSTQHTNPEA\*IVNP GVPNX\*XNSH\*LXCAHCPLSXRETCRASCINESANXRGXAVAYWALFRFL AHDSLRSVXGCGERYQLIKGGNTVIXKSGDNAGKNFXQKAXKGGN\*KAXS **GFFXGPPRXLXKSTHSSGKPK** 

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# FIG. 10

MPELPWVEKYRPKKLSEIVNQEEAIEKVRAWIESWLHGHPPKKKALLLAG
PPGSGKTTTVYALANEYNFEVIELNASDERTYEKISRYVQAAYTMDILGK
RRKIIFLDEADNIEPSGAKEIAKLIDKAKNPIIMAANKYWEVPKEIREKA
ELVEYKRLTQRDVMNALIRILKREGITVPKEILLEIAKRSSGDLRAAIND
LQTVVVGGYEDATQVLAYRDVEKTVFQALGLVFGSDNAKRAKMAMWNLDM
SPDEFLLWVDENIPHLYLNPEEIAQAYDAISRADIYLGRAARTGNYSLWK
YAIDMMTAGVAVAGRKRRGFVKFYPPNTLKILAESKEEREIRESIIKKII
REMXMSRLQAIETMKIIREIFENNLDLAAHFTVFLGLSEKEVEFLAGKEK
AGTIWGKALALRRKLKELGIREEEKPKVEIEEEEEEEEKTEEEKEEIEEK

# FIG. 11

MSEEIREVKVLEKPWVEKYRPQRLDDIVGQEHIVKRLKHYVKTGSMPHLLF AGPPGVGKTTAALALARELFGENWRHNFLELNASDERGINVIREKVKEFAR TKPIGGASFKIIFLDEADALTQDAQQALRRTMEMFSSNVRFILSCNYSSKI IEPIQSRCAIFRFRPLRDEDIAKRLRYIAENEGLELTEEGLQAILYIAEGD MRRAINILQAAAALDKKITDENVFMVASRARPEDIREMMLLALKGNFLKAR EKLREILLKQGLSGEDVLVQMHKEVFNLPIEEPKKVLLADKIGEYNFRLVE GANEIIOLEALLAQFTLIGKK\*\*

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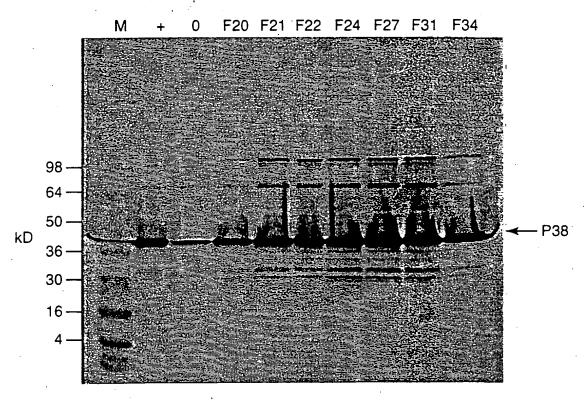


FIG. 12A

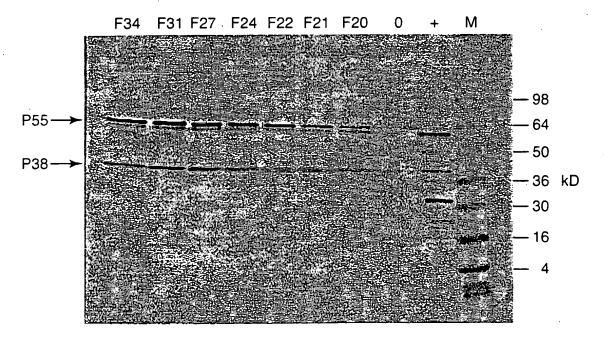


FIG. 12B

USE

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**WASHES** 

pH 2.8 ELUATES

αP38 αP55 F18 F19 F20 F21 F22 F23

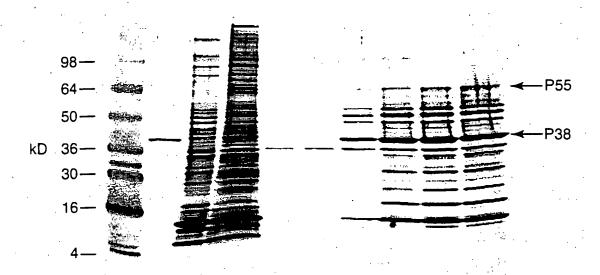
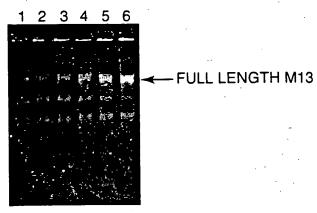


FIG. 13

#### NATIVE CLAMP LOADER STIMULATION OF cPfu/CLAMP PRIMER EXTENSION ON M13



#### **VOLUME OF NATIVE CLAMP LOADER**

- 1. 0
- 2. 0.01ul
- 3. 0.1ul
- 4. 0.5ul
- 5. 1ul
- 6. 2ul

FIG. 15

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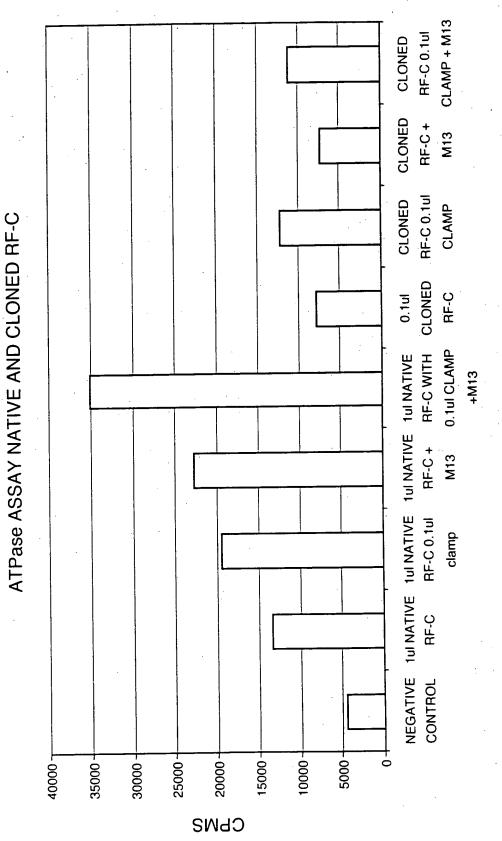


FIG. 14

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# FIG. 16

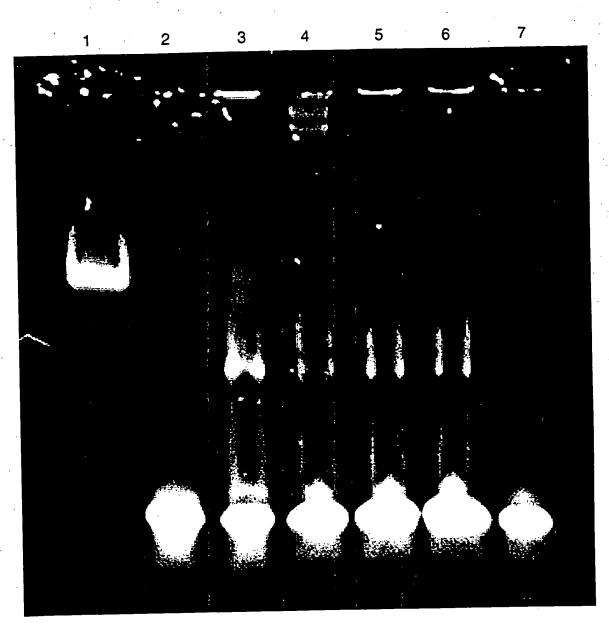
ATGAGT7GCATTTACAAAAGAAGAAATAATCAAGAGGATCCTGGAAGAAG TGGAAGGAATAACTCTAGAAGAAATTGAGAACCAAATAAGGCAAATAATG AGGGAAAACAATATTTCAGAGCATGCAGCTGCTCTTTACTAGCAGAAAG GCTGGGAGTTGAAGTTACCAAAAGAGAAGAACAACCTTTAATGAAGATTA GCGACCTATATCCAGGAATGGATCCCCACGAGGTCAACATTGTTGGAAGA ATACTTAAGAAGTATCCACCGCGAGAATACACAAAGAAGGATGGAAGCAT TGGAAGGGTTGCCAGTCTAGTTATATACGATGATACTGGGAGAGCGAGGG TTGTTCTTTGGGATTCAAAAGTTTTTGGAGTATTACAGCAAGCTAGAAGTA GGGGATGTTATTAAGGTTTTAGACGCCCAGGTTAGGGAGAGCTTATCTGG TTTGCCTGAATTGCACATTAACTTCAGGGCTAGAATAATTAAAAACCCAG ATGATCCTAGGGTTCAGGATATCCCACCTCTTGAAGAAGTTAGAGTGGCA ACTTATACGAGAAAGAAGATCAGTGAGGTCGAGCCTGGGGATAGATTTGT AGAGCTTAGGGGAACAATTGCCAAAGTTTACAGAGTTTTGGTATATGATG CATGTCCAGAGTGTAAGAAGAAGGTTGACTATGACCCAGGAATGGACGTT TGGATATGTCCAGAACATGGAGAGGTTGAGCCAATAAAAATCACTATTCT TGACTTTGGGCTTGATGATGGCTCGGGATACATTAGGATTACCCTCTTTG GAGACGATGCTGAAGAGTTGCTGGGAGTAGGGCCAGAAGAGATTGCCCAA AAGCTTAAGGAAATGGAGAGCATGGCCATGACTCTCAAGGAGGCAGCGAG TGAGGGGAAATGTAATTGAGGACAGGTTCTTGGGCCTAATCTTAAGGGCC TCCTCCTGGGAAGAAGTTGACTACAAGAGAGAAATTGAGAGAATTAAGAG GGAATTGGAAGAATTGGGGGTGATGTGA

### FIG. 17

MI3MSAFTKEEIIKRILEEVEGITLEEIENQIRQIMRENNISEHAAALLLA
ERLGVEVTKREEQPLMKISDLYPGMDPHEVNIVGRILKKYPPREYTKKDG
SIGRVASLVIYDDTGRARVVLWDSKVLEYYSKLEVGDVIKVLDAQVRESL
SGLPELHINFRARIIKNPDDPRVQDIPPLEEVRVATYTRKKISEVEPGDR
FVELRGTIAKVYRVLVYDACPECKKKVDYDPGMDVWICPEHGEVEPIKIT
ILDFGLDDGSGYIRITLFGDDAEELLGVGPEEIAQKLKEMESMGMTLKEA
ARKLAEEEFYNIIGKEIIVRGNVIEDRFLGLILRASSWEEVDYKREIERI
KRELEELGVM

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RFA GEL SHIFT

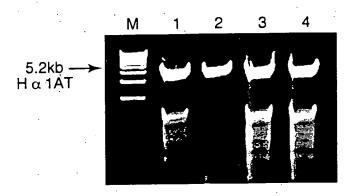
FIG. 18

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#### Pfu TURBO WITH RFA

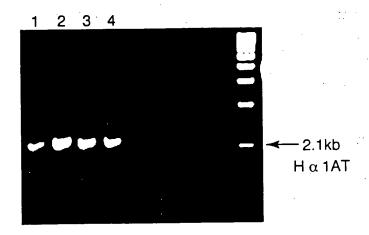


#### RFA/50 µI PCR RXN

- 2. 1µ1
- 3. 1*µ*11/10
- 4.  $1\mu$ l 1/100

FIG. 19

#### Pfu TURBO WITH RFA



#### RFA/50 µI PCR RXN

- 1. 0λ
- 2. 1λ
- 3.  $1 \lambda \text{ of } 1/10$
- 4.  $1 \lambda$  of 1/100

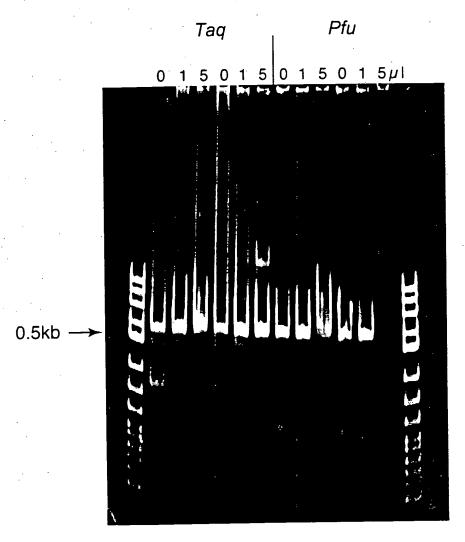
FIG. 20

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# EFFECT OF RFA AND E. COLI SSB (PERFECT MATCH) ON PCRs USING Taq AND Pfu DNA POLYMERASES



RFA = P. FURIOSUS RFA PM = STRATAGENE'S E. COLI SSB

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# FIG. 22

ATGATTGAGGAGCTGTTCAAGGGATTAGAGAGTGAAATCGTTGGACTTCA CGAGATTCCCCCAAAGAGGGGAGGAGTATGGGGAGTTCAAATTCAGGAATG AAGAAGTTAATGAGTTAGTTAAGAGGCTCGGATTTAGACTTTATTCTCAC CAAGTTAAAGCCCTAGAAAAGCTGTATTCAGGGAAAAACGTAGTTGTTTC AACGCCCACAGCTAGTGGGAAAAGCGAGATATTTAGGTTGTTTATCTTTG ACGAAATACTGTCAAGCCCGTCCTCAACTTTTCTCTTTAATCTACCCAACA AGAGCCTTAATAAACAACCAAATGGAAAAATTCGAAAAAGAAAACACTAT CTTTGAGGAGATTTGTGGAAAAAGAGTTCGAGCAGAAGTCTTAACTGGAG ATACGGAATGGGAAAAGAGAAGAGAAATCATTAGGAGCAAACCAAACGTA ATCTTCACGACACCCGATATGCTTCATCATCACATTCTTCCCAGGTGGAG GGATTATTTCTGGCTTTTAAAGGGGCTTAGACTTCTTGTCGTGGACGAAT TGCACGTTTATAGGGGGATCTTTGGAACAAATGTTGCTTATGTTTTCAAG AGACTCTTTCTCAGGCTTAAGAGATTAAGTTCAAGCCCCCAAATACTTGC CCTTTCAGCAACTTTGAGAAACCCCCAAAGAATTTGCTGAACAATTTTTTTG AGACTGAATTTGAGGAGGTCAAGGAAGCTGGAAGTCCAAGCCCGAGAAGA ATTATAGTCATGTTTGAGCCAAGAAGGTTTACTGGAGAACAACTAATCAA GCAAATTGTTGAGAGACTAACTAGAAAGAACATAAAGACCTTGGTATTTT TTGACTCCAGAAAGGGGACAGAAAGAATCATGAGGCTTTTCCTGTTCTCA AAGGTTTCTAATAGAGAGAGACTTTAGGGAGGGCAACCTCACAGTTCTCC TAACGACAAATGCACTCGAGTTGGGAATTGACATTGGAGATTTAGATGCA GTAATAAACTATGGGATTCCTTCAGATGGATTGTTTTCACTAATTCAAAG ATTTGGTAGGGCCGGAAGGGATCCAAATAGAATTGCAATAAACGGGATAA TTTTGAGAAGAAATGGATTGGACTACTATTACAAAGAACATTTCGATGAG CTCGTTGAGGGAATAGAAAAGGGCCTAGTGGAGAAAATCCCCGTTAACTT GGACAATGAAAAGATAGCGAAAAAGCACCTCCACTATGCCATAGCTGAAC TTGGAGTTGTCTCAATTAAAGAAATTGAGGGGAGATGGAAGAGATTCATA AAGACCCTCGTAGAGGAGGGATACGTGGAAGTTACAAGAAATCCAATAAC TGGAGAGAAATAAGACTCAGAAGACCTCCTGTCTATTCTTCAATTA GAACGGCGAGCGATGAAAGCTACTTCTTAGTCGTGGATGAACCCTGGATA AGGGGAGCTTTGCAGAGGAAGAGGGGAGCCGAACTTCTCCGTTTTGTAAA CTACCTCAAAGTTAGAGGAATGGTAGTTGAGGAAGTTGATGAGATAGAAT TCCACAGAAGTCTACTCCCTGGAATGGTCTACCTTTCAAGGGGAAGGCCC TACATGGCAGTTGATAAGATAAAGATTGAGAAGTTCCACTTCGTTTTTTGC GAGGCCTCTTCCAATCGAAGAAGAAATAGATACTAGTTCAAGTAAAATTG AAAACATTGAGATACTTGAGGTTAAAGACGAGAAAACTGTTGGCCCAATA AAAGTGAAGTTCGGAAGACTTAGAGTAAGGCACGAATACACTGGATACGC CGTGAGGGGAAGAGACGTTGAAAGGCACGTTAAGAGATTAGAAGAGCTAA AAGATGAGGGGATACTAAGGGGAGAGATTGACATCGTCCCATACATTTGG GAATCCTGGAAGTTTGCGAGGGTACTCTTTGACACCCCCTACATTAGAGA GTTTGAAACTGAAGGTTTCTGGCTTGAGTTTCCAAACGATATTAGGATAG CCAGAGCTCGCGATGTTCCTCTACAACAGAATTAGTAGAAAATCTCTATT CCCCACGCTTCTGGGAGCAACCACACACTACATAAGGAGTTTCATCCTTC (cont.)

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# FIG. 22 (cont.)

ACCACGCCAAAGATAAGGGAGAAGAATTCGCATTTGCCGTAAAAAAAGATG ATCGACAGCAAGGATGGGATAGGCTCAGGGCTTCATGCAATTGAGCCCAA TATAATAAAGCTTGCTCCAGTTGTGACTCATGTGGATTCGAGAGAAATAG GCGGCTACAGCTACGATGACTTCCATGGAAAGCCAGTGATCTTCATCTAT GATGGGAATGAAGGCGGAAGCGGAATAATTAGGCAGGTGTATGAGAACGT AGAAAAGCTGATGTACAGGAGTTTGGAGCATATAAAGAAGTGTCCATGCA AAGACGGCTGTCCTGCCTGCATATATTCTCCCAAGTGCGGAACTTTCAAT GAATTCCTCGACAAGTGGATGGCAATAAGAATATGGGAAAAAGTCCTTCC

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# FIG. 23

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ATGTTAATAGTTGTAAGACCAGGAAGAAAAAAGAATGAGCTCGAGGCTTTTA TAATTGAAAACCCTCCAGAAAAGCTCTCTCAAAGAAGAAATTTAAAAGCTGA TAGGGTAGTTAGGCTCATAATGAGAGATAATAGACTTTTTAAAGCTCTTGAA GGAAGTCAGTATTTAAATCCAAAGGAAGTGGAGAGAGCCCTTAGAAATTCAA GGATAGTTCTGGTGAATGCCAACGAGTGGGAAGAGTACTTTAAGAAGAGGTT AATGAACAAAAGAGTTGAAAAAGCTGACATCTGTAGGCTCTGCCTTCTCAAT GGGAAGATTACAGTACTCACTGAGGGAAACAGGATAAGATACAGAGATGAAT ATTTAATTCCATAGGAATGCTTGAACAGGCAAAGAAGCTTTTAGAGAGATTC AGAGATTTAGACAAGGTGATTTCAATTTTTGATCCATCCTTTGACCCCACTA AGCATCCAGAGATAACAAAATGGGATGAGCTAAAGGCCAAGCATATAAGGGT CGAGAAGATGCATATAGATGAGCTCAACATCCCCGAAGAATTCAAAAAAGTT CTAAAGGCCGAAGGAATAAACGAACTACTCCCCGTTCAGGTGCTAGCGATTA AAAACGGCCTCCTAGAGGGGGAGAATTTATTGGTGGTTTCAGCAACTGCGAG TGGAAAAACTCTAATCGGAGAGCTTGCAGGTATTCCTAAGGCTCTAAAGGGA AAGAAAATGCTGTTCCTAGTTCCTCTAGTAGCTTTAGCAAACCAAAAGTACG AGGACTTCAAGAGAAGATACTCAAAGCTTGGATTAAAAGTAGCCATTAGAGT CGGAATGAGCAGGATAAAGACCAAGGAAGAGCCAATAGTTCTGGATACTGGA ACAGATGCACACATAATAGTGGGGACTTACGAAGGAATAGACTACCTTCTCA GAGCTGGTAAAAAGATAGGAAACGTTGGAACGGTTGTAATAGATGAAATACA CATGCTCGATGATGAGGAGAGAGGAGCTAGGCTAGATGGGCTCATTGCAAGG TTAAGGAAGCTCTATTCAAATGCCCAATTTATTGGGCTTTCAGCAACCGTAG GAAACCCTCAGGAGTTAGCCAGGAAGCTAGGGATGAAACTAGTGCTTTACGA TGAAAGGCCCGTTGACTTAGAGAGGCATTTAATAATTGCGAGAAATGAGAGT GAGAAGTGGAGGTATATAGCTAAGCTGTGCAAAGCCGAGGCCATGAGAAAGA GCGAGAAGGGATTCAAGGGGCAGACGATAGTATTTACATTTTCAAGGAGAAG ATGCCATGAGCTTGCCTCATTCCTAACGGGGCAGGGATTGAAGGCTAAGGCC TACCACTCGGGCCTCCCCTATGTTCAGAGAAAGCTTACCGAAATGGAGTTTC AAGCTCAAATGATTGATGTAGTTGTAACAACAGCTGCTTTAGGAGCGGGAGT TGATTTTCCAGCATCCCAAGTCATCTTCGAAAGCTTGGCCATGGGAAACAAG TGGATAACAGTTAGGGAGTTTCACCAAATGCTTGGCAGGGCTGGAAGGCCAC AGTACCATGAGAAAGGTAAAGTTTACATAATAGTCGAGCCTGGGAAAAAGTA CTCAGCTCAGATGGAGGGAACTGAAGATGAAGTCGCCCTCAAGCTCTTGACT TCACCCATAGAACCAGTAATTGTTGAGTGGAGCGATGAATTTGAAGAGGATA ATGTCTTAGCTCATGCCTGTGTGTTTAATAGACTTAAAGTTATTGAAGAAGT TCAATCCCTCTGCCTGGGAGCAAACCAAAGTGCTAAAAATGTTTTGGAAAAA CTTATGGAAAAGGGGCTCGTCAAAATATATGGAGATAAAGTTGAAGCAACCC CATATGGAAGGGCGGTGAGCATGAGTTTCCTACTTCCTAGGGAGGCAGAGTT CATCAGAGATAACTTGGAGAGCACTGATCCAATTGAGATAGCAATTAAACTG CTACCGTTCGAAAACGTTTACCTCCCAGGATCGCTCCAGAGGGAAATAGAGT CAGCTGTTAGAGGAAAGATAAGCTCAAACATCTTTTCAAGCTCCTTTGCATC AGTGCTAGAAGAGCTTGACAAGATTATACCCGAAATAAGCCCAAATGCTGCA GAAAGGCTATTCCTAATATACCAAGATTTCTTCAACTGCCCAGAGCAAGACT GTACGGAGTTTGCAATGGAGAATTGGGAGAAAGATCATTGACTTAAGAAG AGAGGGATACGAGCCCTCAAAAATCTCTGAGCACTTTAGGAAGGTCTATGCA TTAATATTATACCCTGGAGATGTTTTTACATGGTTAGACGGAATTGTGAGAA AACTCGAGGCAATTGAAAGAATAGCCCGAGTGTTCAATAAGAGAAGAGTGGT AGAAGACACAATCAGGGTTAGAAGGGAAATTGAAGAAGGAAAAATTTTGAAG GGTGAGAGACGATGA

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### FIG. 24

ATGCACAAATACTTCTTTCCATTACCTGCAACTAAGTCAACTTTCTTGCTC CCTGCCGACCTCACCACAGCAAATCCATGCTTTTCCAAGAGCTTAATCAAT TCTCTCTCTGCCTGGGCCCCTTTTCTATACATACAATGTTTTTCCTATCTA CCTCTTATAAACTTTTTAAACTCCTTGACATACCCTCTCGAGATGCACATA TTGATAAAAAGGCAATAAAAGAGAGATTTGGAAAGTTGAATGCCCTTCAA CAATTAGCCTTTCATAAAATTAGGGGAGAAGGTAAAAGTGTTTTAATAATA GCTCCGACAGGAAGCGGAAAAACTGAAGCCGCAGTAATTCCAATCTTAGAC GCAATACTACGGGAGAATCTTAAACCTATAGCAGCTATTTATATAGCCCCA TTGAAGGCACTAAATAGGGACTTGCTAGAGAGACTAAAGTGGTGGGAAGAA AAAACTGGGGTAATAATAGAGGTTAGGCATGGGGACACGCCTACCTCAAAA ATGCTCCCTGCTATTCTTACGACAAAGTCCTTCCGTCCCTATCTTAAGAAC ACTAAATTTATCGTGATAGACGAGATTGGTGAACTTATAGAGAATAAAAGA AAACCAATAAGGATTGGCCTTTCTGCAACAATTGGAAGTGAAGAAAAGGTA AGGCTTTGGATGGAAGCGGATGAAGTGGTAAAGCCTCGACTAAAAAAGAAG TACAAATTTACCGTTTTATACCCTCAGCCAATTCCAGAGGATGAAAAGCTT GCTGAAGAGCTCAAAGTTCCAATAGAAGTTGCAACGAGGCTAAGAGTTGTG TGGGATATTGTAGAAAAGCACAAGAAGGTATTGATCTTTGTTAATACCCGA CAATTTGCAGAGATCTTAGGGCATAGACTTAAAGCTTGGGGAAAACCTGTT GAAGTTCACCATGGTAGCCTTTCAAGGGAAGCAAGAATAGAGGCAGAGAAG AAACTTAAGGAAGGAAAAATAAAAGCACTAATTTGTACCTCATCAATGGAA CTTGGCATTGACATAGGGGATGTTGATGCAGTTATTCAGTACATGAGTCCT CGACAGGTAAATAGGCTAGTCCAGAGAGCTGGAAGAAGCAAACATAGACTG TGGGAAACAAGCGAGGCTTACATCATAACCACAAACGTAGAAGATTATCTC CAAAGCTTGGCAATAGCAAAGCTCGCACTAGAAGGAAAACTGGAAGATGTA AATCCCTACGAAAATGCCCTTGATGTCCTGGCTCACTTTATAGTTGGTTTG ACAATAGAATACAGAAATGTTAACATTACTGAACCCTATTCCCTTGCGAAA TCTACTTATCCCTACAGAAAGCTCTCCTGGGAAGACTATCAGAAAGTTTTA GAGATTTTAGAAGAGGCTAGAATAATAAGAAGAGATGGAGATGCAATTAAG CTGGGAAAAATGCCTTTAAGTATTATTTCGAGAACCTCTCAACAATACCT GACGAAATAAGTTATGCAGTTATAGATATTGCAAGTGGAAAATCTGTTGGA AGACTAGATGAAAACTTTGTTACGGAACTTGAAGAGAGTATGGAATTCATC ATAAAGGTTAAGGAGAGCAACAATTTAGAAAGTGCACTGCCAAGTTGGGAA GGGGAGCTCATTCCAGTTCCTTTGGAAGTTGCAGAATTTGTTGGAAAGCTG AAGAGAGAGCTCCTATGGGACAAAGAGAGAGCATTAAAACTGCTTGAGGGC GTTGAATTTAATAAGGAAGAACTCGAGGTTGCAATTTCCCAACTAGTAGAA TCAGAACCAGTGGCGAGTGATAGAGATATCATTATAGAATCCTATCCAAAA TTTGTGATAATTCATGCTGATTTTGGAAATAAAATTAACGAAGGGCTCACA AGATTTATCTCAGTGTTTTTATCCGCCCGATATGGGAATATTTTCCTCCCA AGAAGTCAAGCTCATGGAATTATAATTAGAAGCCCATTTAGGCTTAATCCT GAAGAAATAAAGGAAATACTGTTAATGAAAGCAGAAGTTGGAGATATTGTT GCTAGAGGAATTAGAGACACTCCAATATACCGCTGGAAGATGAGTGCAATT GCTAAGAGATTCGGTGCCCTAAGAAGGGACGCGAGAATAAAAAAAGTAGAA AGGCTGTTTGAAGGGACAATAATAGAGAAGGAGACTTTTAATGAAATTTAC (cont.)

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# FIG. 24 (cont.)

CATGATAAAATCGACATTGATAAAACAGAGAAAATTCTAGAAAAAAATAAGA
AAGGGAGAAATTAGAATGAAAACTTTGTTCAGAGAGGAAAATAACGCCTCTT
TCCTCTTCTTTGGCAACCCTAGGAGGAGGAGTTTCTAATTAGAGATATACTT
ACCCAGGAGGAAGTAGAAGAGATATTTAGGGAGAAGTTACTCGATGCTGAG
TTAGTCATGGTTTGTACAAACTGCGGATTTTCCTGGAGAACAAAAGTTCGC
AGGGTTATGGATAGAGTCAATGAGTTAAGCTGTCCCAAGTGTGATTCCAAA
ATGATAGCTCCTCTACACCCCAAAGATTCCGAAACTTTCATCTCAGCTCTC
AAAAAGTTAAAAAGAGGAGAAAAGCTTAGTAGGGAAGAAAAAGTATTAC
CTTAGAGGTTTAAAGGCGGCTGATTTACTTAAAGCCTACGGGAAGGACGCT
CTTTTAGCATTAGCTACCTATGGGGTTGGGGTAGAAAGCGCCACCAGAATA
CTTAGGGATTATAGAGGAAAATCCCTTATAAAAGCACTTATCGAGGCAGAG
AAACACTACATCCAAACTAGAAAGTTTTGGGAATAG

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### FIG. 25

GTGATGTTATTAAGGAGAGACTTAATACAGCCTAGGATATATCAAGAGGTA ATATACGCCAAGTGCAAAGAAACAAACTGCTTGATTGTTCTGCCCACAGGA TTAGGTAAGACGCTGATAGCTATGATGATAGCAGAGTATAGATTAACGAAA TATGGCGGAAAAGTTCTAATGCTCGCCCCCACTAAGCCTCTCGTTCTTCAA CATGCGGAAAGTTTTAGGAGGCTATTTAACCTCCCTCCAGAAAAAATTGTA GCACTTACTGGAGAGAGAGCCCAGAAGAGAGAAGTAAGGCCTGGGCGAGA GCAAAAGTAATTGTAGCCACTCCTCAAACTATTGAAAATGACTTATTGGCG GGAAGAATATCTTTAGAAGACGTTTCGCTAATAGTATTCGATGAAGCTCAC AGAGCTGTGGGCAATTACGCTTACGTCTTTATAGCAAGAGAGTATAAAAGA CAGGCCAAAAACCCACTTGTTATAGGGTTAACAGCCTCCCCTGGGAGCACT CCTGAAAAGATCATGGAGGTAATAAATAACTTGGGAATTGAGCATATTGAA TACCGCTCCGAAAATTCTCCCGATGTTAGACCTTACGTTAAGGGAATAAGG TTTGAATGGGTTAGGGTTGATCTCCCAGAAATATACAAGGAAGTAAGGAAA CTTTTAAGAGAAATGCTTAGAGATGCCCTTAAACCGTTGGCAGAAACTGGA CTTCTTGAATCTTCTTCCCCAGACATTCCAAAGAAAGAAGTTCTTAGAGCT GGGCAAATAATAAACGAAGAAATGGCGAAAGGTAATCATGATCTCAGAGGC TTGCTTCTCTATCACGCAATGGCTCTTAAGCTACATCATGCAATTGAGCTG TTGGAAACCCAAGGGTTATCCGCCCTGAGGGCTTATATAAAGAAGTTGTAT GAGGAGGCAAAAGCGGGATCAACAAAGGCTAGCAAGGAAATATTCTCGGAT AAGAGAATGAAAAAGGCAATCTCACTTTTAGTTCAAGCGAAGGAGATTGGG CTTGATCACCCCAAGATGGACAAGTTAAAAGAAATAATTAGGGAACAACTC GCAAAAAAGATAGTCAATGAACTTGTGAAAGATGGAATAAAAGCTAAAAGG CAGAAATTAATTCTTGACGAATTCGCTAGAGGAGAATTCAACGTTCTAGTG GCAACGAGTGTAGGAGAGGAAGGACTTGACGTGCCGGAAGTTGATTTGGTT GTGTTTTATGAGCCAGTACCATCTGCCATAAGGAGCATCCAAAGAAGGGGGT AGAACTGGCAGGCATATGCCGGGGAGAGTTATAATCCTAATGGCCAAGGGG ACTAGAGATGAAGCATACTACTGGAGTTCCAGGCAAAAGGAAAAGATAATG CAAGAGACAATAGCTAAGGTGAGTCAGGCAATTAAAAAGCAGAAGCAAACT TCTCTAGTTGATTTTGTGAGAGAAAAAGAGAGCGAAAAGACCTCTCTAGAC AAGTGGTTGAAAAAGGAAAAAGAAGAAGCAACTGAAAAAGAGGAAAAGAAG GTAAAGGCTCAAGAGGGTGTAAAAGTCGTCGTAGATAGCAGAGAGCTTAGG AGTGAGGTTGTGAAGAGACTTAAACTTCTTGGTGTAAAGTTAGAGGTTAAA ACGCTCGATGTGGGAGATTATATAATTAGTGAGGACGTTGCAATTGAGAGG AAGTCAGCTAACGACTTCATTCAGTCAATTATTGATGGTAGACTTTTTGAT CAAGTTAAGAGGCTCAAAGAGGCATACTCAAGACCGATAATGATAGTCGAA GGTTCTTTATACGGAATTAGAAACGTCCATCCAAATGCAATAAGGGGGGCA ATAGCAGCGGTAACCGTAGACTTTGGGGTCCCAATAATATTTTCATCTACT CCAGAGGAAACCGCTCAATACATCTTTCTAATTGCAAAGAGGGAGCAAGAG GAGAGAGAAAACCTGTGAGAATTAGAAGTGAGAAGAAGGCCCTTACCCTT GCCGAGAGGCAGAGGTTAATAGTTGAGGGATTACCTCACGTCTCAGCAACT CTAGCTAGGAGATTGTTGAAGCACTTTGGAAGTGTGGAAAGGGTATTCACT GCAAGCGTTGCTGAGTTAATGAAAGTTGAAGGCATAGGAGAGAAGATTGCT AAGGAGATTAGAAGGGTAATAACTGCCCCATATATAGAGGATGAGGAGTAG

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### FIG. 26

TTGAAAGGGTTGTTTAGGGACGTTATCCTCCACAACCCCCACCTTTTTGTT TATTCCTATTCTGATAAAGGCATCATTCCTTTCAAGCATCAGTTCCAGACC CTCTATCATGCCATGCTCATGAGGCCAGTGAGGCTAATGATAGCTGATGAG ATAGGTCTCGGAAAGACCATTCAAGCTCTTTTAATAGCCAAGTACCTCGAT TTTAGGGGAGAGATTGAGAAAGCCTTGATAGTCGTTCCAAAAGTTCTGAGG GAGCAGTGGAGGGAAGAAGTAAAGAGGATCTTAGAGGAAGCTCCGGAAGTG ATAGAGAATGGTAGCGAAATTGAATGGAAGTTGAAAAGGCCGAGGAAGTAC TTCATAATATCAATAGACCTAGCTAAGAGATACACCGAGGAAATACTCCGT CAAAAGTGGGATTTAGTAATAGTTGACGAAGTCCACAACGCCACCCTGGGA ACACAGAGATATGAGTTCTTAAAAGAACTAACCAAGAACAAGGATTTGAAC GTTATATTCCTTTCAGCAACCCCCCACAGGGGAAACAATAGAGATTACCTT GCGAGGCTTAGGCTCCTCGACCCAACTATACCAGAGGAAATATCCCCAATG CACGAAAGGAAGATCTACATGAAGTCAAGAGGGACATTGGTACTAAGGCGA ACTAAGAAGGTTGTCAACGAACTTGAAGGAGAAGTGTTCAAGAAGTGTCAC TTTGGGGCTGTCGTGGTAGAAGTTAGCAGAGAGGGAGAGGGAGTTCTTTGAA GAGTTAAATAGAGCGCTATTCGAGCTGATTAAGGATCAAGCTGATTACTCT CCCTTAACTCTTCTTGCAGTAATCATTAGGAAGAGAGCCTCGTCCAGCTAC GAAGCGGCTCTAAAAACCCTAACCAGGATCGTTGAAAGCGCTTATATAAGT GGGCAAGAAGAGCCAGAGGCGTTGAATCATACATTGAAAAGATCTTTAGA ATACACAAAATAATAGATGAATATAGGGGATTCTTAACTGAAGAGCAACTC GAAAGGCTTAGAAGAGTTCTCGAGCTTGGAAAGAAAATTGGCAGCAAGGAT AGCAAGCTTGAGGTTATATCCGATATAGTTGCTTATCACATTAGGAACGGC GAAAAGGTCATAATATTCACGGAATTTAGAGATACCCTCGAATACGTACTT GAGAGGTTACCAGATATCCTAAGGAGAAAGCACGGCATTGTTTTGGAAAAA GATGACATTGCAAAACTTCATGGGGGCATGAAATCTGAGGAAATAGAGAGG GAAATCAACAAGTTTCATGAAAGGGCTAACCTATTAGTCTCTACGGATGTT GCATCCGAAGGACTTAACCTGCACGTTGCAAGTGTTGTAATAAACTACGAG GCCCCTGGAGCCCAATAAAGCTCGAACAGAGGGTGGGAAGAATATGGAGG CTCAACCAAACGAGAGAAACCAAAGCATATACCATATTTCTTGCAACGGAA ACGGACTTGGATGTTCTAAACAACCTCTATAGAAAGATTATGAACATAAAG GAAGCCGTGGGAAGTGGACCCATTATTGGAAGGCCAATATTTGAAGGAGAC TTTGAAAATCTATGGAATGAAGGTGCCGAGGAAGAAAATAGAGAAGTCTCA GAGTATGAGCTTATCCTAGCCTCAATTAAGGGAGAACTCAAGGGCTATGCC GTTCCTGTAAATCCTGCGGGAAGCATAAGGAGAGAGCTCGAGATAATTTTA GAGGACACTCCTGATGTGGAAGTATTAAAGAAAATCGTTAATAGGAACGTT CCAAATCCGTTCCGCTTGGTGAGAGGACTTTTAAGAGAAGCCGAGGGGATT GAGGGAATTAGAGTATTAGTTAAGGGCTATGATGGCTCTATGGATGTGTAC TATGCCATATTCTACGACGAAGATGGGAGAGAAATTTATAGATATCCAATT CTTGCTGAGAACGGAAAGTACCTTGTTGGATTCAACTTACTCAAGAGGATT AGTGAGGTACTATCCAAAGAGTACAAGGTCGTTAGAGGGGCAAGTGAAGAG GTGGACTATAAAGTTAAGACGCTAGTTATGGACAACATATACAATTTAATC GTGAAGAAGTATCTGGAATACGATAGCTTAAACATCAAAGAAGGTAAAATC TTCAAGAGGCTTAAGGTTGAAATAAAGAAAGCCCTCGAGGTAAAGGGGATA (cont.)

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# FIG. 26 (cont.)

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### FIG. 27

GTGATTACTTTGGAGCTACATCCAAGTGAGATAGCTAGATATTTCGAGCTT TTGCAGGAATTTGAGCCGATAATAAGGAGAAAAGAAATAGAAACCATAGAG CTCGCCAAATGGGGAGACGAGTTCGAGCTCTCCCTTCTTCAGGAATTTAAA AAAGGTGAAGCATTAAAAAAGCTTGGAGTTAAAGAACTACCAAGATTCTAT GGTTTTTTAACGGAAAACGACACCCCTGTAAGAAAGTTCTTTGAAAAGTAC TTTAAAGATGGAATAATAGTGGAAGAAGATCCAGACAAACTTTTAGAAATT ATAAACAGTGAGAAAAGTGCCGTTATCTATCAAGCCCCCTTAAAAAGGCAGA ATAGGGAAATTTGATGTCTCAGGAAGGGCAGACTTCATAATAAAGGTTGGG AAAACACTTTACCTACTCGAGGCTAAGTTTACTAAGGAAGAGAAGTTCTAC CACAGGATTCAGGCCATTATCTATGCTCACCTTCTAAGTCAAATGATCGAA GGTTACGAAATTAAACTAGCTGTTGTAACAAAGGAGAACTTTCCCATTCCC TCAAACTTCCTAAGATTCCCAGGAGACGTGGAAGAGTTAAAGATAACCCTA GAAGAAAAGCTTGGTGGAATACTAAGAGAACAAGAACTTTGGATAGACGCA AGGTGTACTACTTGCCCCTTTGAGGCTTTATGCTTGTCTAAGGCTCTTGAG GAAAGAAGTCTAGGACTATTAAGCCTTCCCCCTGGGATAATTAGAATACTC AAAGAAGAAGGGATAAAAGACTTAAAAGACATGGCTAAGCTATTTGAATTC AAAGAAAATTCCCCTACAAACTTTGAAGAGCCCTCAATAAAAGATCCAAAG AAGACTCAAGAGATAGCAAAAAGAACGGGAATAAACTTACTAAAGCTCTCA AGGATAGCTCAGGCAATCCTTAAATATTTAGATGAGGGAGAAACAACACCC CTGTTCATCCCCAGGACGGGGTATAATCTGCCAATGGATGAGAGAGTAGGT GATGTTGAGCCCTCTTACTATCCTCCAAGGAGCTTAGTGAAAGTGTTCTTC TATGTCCAGACAAGCCCAATAACAGACACAATAATCGGAATTTCAGCCCTT GTAAAGAATAGGCAAAATGGAGAGCGGATAATTGTTAAGTTCGTCGATGAG CCCCCATAGAAGTTTCAGATGCCCAAGAAAAGGAGAGAATGCTTCTAATT GAGTTCTTTAGGGATGTTATTGATGCCGTAAAGTCACTATCTCCAACCGAT AAAGTCTACCTACACATGTACTTTTACAATAGAAAACAGAGAGATGACCTT ATGGATGCCGTAAAGAGACACAAAGAGATAAGAGAAAACAATGCAGTCATG GCCTTGCTAAGCTTGAGAAGAGCCATAGATTGGGAGAGCTTTTCAATAATA AAGGATGAGATAATAAGGAGGCATGCCTTACCACTTTCTCCTGGCCTGGGA TTCGTTACAGTTGCTACTCAGTTTGGATACAGATGGAGAAGGAACAAAACC TTTGCGCGAATGCTTGAGGTTGTAGCAAGAAGAGAAAATGGTAAGATAAAT CTCAAAACTCTCCTTAACATTTCTGAAACGGGAATTGGGCCAGAATATTAT CCAATCATCGATAGGGATAACGAAGGAATACCCTTCACACTTTTCTGGAGC GCACTGGTCAAATTAGCTACTGAGGAAGACAATTCAAGAATTAAGAGGGAT ATAAGGGACATACTCTCCCAAATGGTTGAGGCCCTCAAAACAATTGAAGAG AGAATTCCCGAGCAATATAAAGACGCCTTCGTGAAAAAAGAGGGGAATACCC AAAGAAGATCTCGAAAACTTTGACATAAAGAAGGAAGAATTAGCTGATATC CTTCTTGAATACTTACAATTAGAGTTCGATGCAAGATTTAGAGAACGATCC GAATACTATAGGCTTCCCCTATCAATAAGAGCATACTCAGAGGAATCAGCA GGAAAAATCGTGCTAATTGACGAAAATGGAAGAATAAAAGAGTATAATCCA AAAGAAGTTCTTATAGATATTGATGAAGGTTCTCTTGTAGTTGTAACGCCA AAGAAATTCTTAGATAAGCTAAGAAGAGATCCCGTTCAAAGAATAAGCAAA TCACCGTTAGGAATAGTTGAGGCTATAGATCACGAGACAGGAAAAGTTGTT ATAAGGTTAATAAGAGTCTCTCCAGGCAGATTTACACTCAAACACTCTAAG (cont.)

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# FIG. 27 (cont.)

TTTAGTTGTAAAAATGGACTATTGACAATAACCTATCCTGAAGGGGAAGTG AAAGTTACTCCTGGAGAGATAGTTATAGTAGATCCTAGCGTCGATGACATA GGAATGGAAAGGGCATACAATGTGCTCTCAGAAATATCCCAAGGGGAACTC AAGCATGAAATTTATCAGAAGGTCAAAGCAATATACGAAGGGAACACGGAA TCAAGATACGAAGTCAACATCTGGAAGAAAAAGCACATAGAAGAATTTCTC TCCAGAGTTAAGAAGATCAACGAAGAACAGAAAAAGTTTGCAATTGACATA AACAACTTTCTAGTCACCCTTCAAGGCCCCCCTGGGACTGGGAAGACATCA GGGGCCATAGCCCCAGCAATTCTCGCAAGAGCATATTCAATGGTGAAGGAC AAAAAGAATGGCCTCTTTGTAGTTACTGGAGTCTCACACAGGGCAGTTAAT GAGGCCCTGATAAAGACTTTAAAGCTAAAGAAAGAGCTGGAGAATACATTA AAAGAGCTTAGAAAGATAGATCTAATTAGAGCAGTCTCTGGGGAAGAGGCA ATCAAAATAATTAAAGAGGAACTAGAGAGGGAAATAAAGGATGATGTCGAC AGAATTAGATTTACAGCACAAGAAATTACCCACTCTTCAAAGCAAAGATCA TTAGACAAATATTTTGCTAATTCTGGAACTGTGAGGATAGTATTTGGAACA CCACAGACTTTGAACAAGCTTATGAAGAATACAAAAGAAGTCGAACTAGTT GTCATAGATGAAGCTAGTATGATGGACTTACCAATGTTCTTCCTCTCAACA AAAGTTTGTAAAGGTCAAGTTCTCTTGGTCGGGGATCACAGGCAGATGGAG CCAATTCAAGTCCATGAATGGCAATTAGAGGACAGAAAGACATTTGAAGAG CACTATCCATTCCTTTCAGCCCTTAACTTCATTAGATTTCTCAGGGGAGAG TTGGATGAAAGAGAACTTAAGAAGTTTAAGAGAATCCTTGGAAGGGAACCT CCAGAATGGAAGAAGGACAAGAACGAGGTTCTCCCTCTATAGGTTAGTA AGAACTTATAGGTTGCCCCAGGAAATAGCTGATCTACTGAGTGATGCAATA TACAGAGCAGATGGCATAAAATTGATTAGTGAAAAGAAAAAGAGAGAAAAG ATAATTGCCAGGCACAAGGATGAGTTTCTATCGATAGTTTTAGATGACAGG TATCCTTTCGTTCTAATACTTCATGACGAGGGCAATTCCACAAAGATTAAC GAGCTGGAAGCAAAGATAGTAGAGAAGATAATCAAAAGAGTAGAGAATATT GATATAGGAGTTGTAGTTCCATATAGAGCTCAAAAGAGATTAATAGCTTCA TTAATAGATAGTGCCCAGGTGGACACAGTTGAGAGATTCCAAGGGGGAGAG AAATCTTTAATAGTAATTTCAATGACTTCCAGCGACCCCCGCATACCTGGG AAAGGTTTTTGA

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# FIG. 28

ATGAACATAAAGAGCTTCATAAACAGGCTTAAGGAGCTAGTTGAAATCGAG AGGGAAGCTGAAATAGAGGCTATGAGGTTGGAGATGAAAAGGCTTAGCGGA GTGGAGAGGGAGAGGTTAGGTAGGCAATTCTCAGCTTAAACGGTAAAATC ATAAAGACCGAGATCAGCGTTGGGGATTTGGTTGTTATAAGCAAGAGGGAT CCCCTGAAGAGCGACCTCCTGGGAACTGTTGTTGAGAAGGGGAAGAGATTC ATCGTCGTTGCCTTAGAACCAGTCCCAGAGTGGGCCCTTAGAGATGTGAGG ATAGACCTCTACGCCAACGATATAACATTCAAGAGGTGGATCGAAAACCTC GACAGGGTTAGGAAGGCTGGAAAAAAGGCTTTAGAGTTTTACTTAGGTTTA GATGAGCCTTCCCAGGGGGAGGAAGTGAGCTTTGAACCCTTTGATAAGAGC CTAAACCCCTCTCAAAGGAAAGCGATAGCTAAGGCTTTAGGTAGTGAAGAC TTCTTCCTTATCCACGGCCCCTTTGGAACTGGAAAGACGAGGACTTTAGTT GAGCTGATTAGGCAGGAGGTAAAGAGGGGGGAACAAAGTTCTAGCTACAGCT GAGAGCAACGTTGCCGTGGACAATTTAGTTGAAAGATTGGCCAAAGATGGA GTTAAGATAGTTAGGGTTGGGCACCCAAGTAGGGTTTCGAGGCATTTGCAC GAGACAACTTTAGCTTACCTCATTACTCAGCACGAGCTCTACGGTGAGCTT AGGGAGCTTAGGGTGATAGGGCAGAGTTTGGCAGAGAAGAGGGACACATAT ACAAAGCCGACTCCAAAGTTCAGGAGGGGACTGAGTGATGCTGAGATAATT AAGTTGGCCGAGAAGGGAAGAGGGGCTAGAGGACTCTCAGCTAGACTAATA AAGGAGATGGCCGAGTGGATAAAGCTAAACAGGCAGGTTCAGAAGGCCTTT GAAGATGCTAGAAAGCTTGAGGAGAGGATTGCGAGGGATATAATTAGGGAA GCCGATGTGGTTTTGACAACTAACTCTTCTGCAGCCCTTGATGTTGTTGAT GCTACCGATTATGATGTTGCGATAATAGATGAAGCAACTCAGGCAACTATA CCGAGCATATTAATACCTCTCAACAAGGTTGATAGGTTTATACTTGCTGGA GACCACAAGCAACTACCACCAACTATCTTAAGCTTGGAGGCCCAGGAGCTC TCCCACACGCTTTTCGAGGGTTTAATTGAGAAGTACCCATGGAAGAGCGAA ATGCTGACAATTCAGTATAGGATGAATGAGAGGATAATGGAGTTTCCGAGC AGGGAGTTTTACGATGGAAGAATAGTTGCTGATGAAAAGTGTAAAAAAACATA ACTCTGGCCGACCTGGGAATTAAAGTTAATGCTAGTGGAATATGGAGGGAC ATCCTAGATCCAAACAACGTCCTCGTGTTCATAGATACTTGCATGCTCGAA AATAGGTTCGAGAGGCAGAGAAGGGGAAAGCAAAGCAGGGAGAATCCCTTG GAGGCCAAGATAGTGAGCAAAATCGTTGAAAAGCTCTTGGAAAGTGGGGTT AAAGCGGAAATGATGGGAGTGATTACACCTTACGATGACCAGAGGGATTTG ATAAGCTTGAATGTTCCCGAAGAAGTTGAGGTCAAGACTGTGGATGGTTAC CAGGGAAGGGAAGGAAGTGATAATTCTATCATTTGTCCGCTCTAACAAA GCGGGAGAGATCGGCTTTCTCAAGGACTTGAGGAGGCTAAACGTGTCCTTA ACTAGGGCTAAGAGGAAGCTTATCATGATTGGCGATTCCTCAACGCTTTCA TCTCACGAAACCTACAGGAGGTTAATCGAGCACGTGAGGGAGAAGGGGTTA TATGTTGTGCTAACGAAGGATAGCATTTGA

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# FIG. 29

MIEELFKGLESEIVGLHEIPPKRGEYGEFKFRNEEVNELVKRLGFRLYSHQ VKALEKLYSGKNVVVSTPTASGKSEIFRLFIFDEILSSPSSTFLLIYPTRA LINNOMEKFEKENTIFEEICGKRVRAEVLTGDTEWEKRREIIRSKPNVIFT TPDMLHHHILPRWRDYFWLLKGLRLLVVDELHVYRGIFGTNVAYVFKRLFL RLKRLSSSPQILALSATLRNPKEFAEQFFETEFEEVKEAGSPSPRRIIVMF EPRRFTGEQLIKQIVERLTRKNIKTLVFFDSRKGTERIMRLFLFSDAFDRI TTYKGTLTKRERFLIERDFREGNLTVLLTTNALELGIDIGDLDAVINYGIP SDGLFSLIQRFGRAGRDPNRIAINGIILRRNGLDYYYKEHFDELVEGIEKG LVEKIPVNLDNEKIAKKHLHYAIAELGVVSIKEIEGRWKRFIKTLVEEGYV EVTRNPITGEEEIRLRRPPVYSSIRTASDESYFLVVDEPWIRGALQRKRGA ELLRFVNYLKVRGMVVEEVDEIEFHRSLLPGMVYLSRGRPYMAVDKIKIEK FHFVFARPLPIEEEIDTSSSKIENIEILEVKDEKTVGPIKVKFGRLRVRHE YTGYAVRGRDVERHVKRLEELKDEGILRGEIDIVPYIWESWKFARVLFDTP YIREFETEGFWLEFPNDIRIVPEEEFREFFAVASEIDPELAMFLYNRISRK SLFPTLLGATTHYIRSFILHHAKDKGEEFAFAVKKMIDSKDGIGSGLHAIE PNIIKLAPVVTHVDSREIGGYSYDDFHGKPVIFIYDGNEGGSGIIRQVYEN VEKLMYRSLEHIKKCPCKDGCPACIYSPKCGTFNEFLDKWMAIRIWEKVLP

# FIG. 30

MLIVVRPGRKKNELEAFIIENPPEKLSQRRNLKADRVVRLIMRDNRLFKAL EGSQYLNPKEVERALRNSRIVLVNANEWEEYFKKRLMNKRVEKADICRLCL LNGKITVLTEGNRIRYRDEYICESCAEEELKRELRFRFNSIGMLEQAKKLL ERFRDLDKVISIFDPSFDPTKHPEITKWDELKAKHIRVEKMHIDELNIPEE **FKKVLKAEGINELLPVQVLAIKNGLLEGENLLVVSATASGKTLIGELAGIP** KALKGKKMLFLVPLVALANQKYEDFKRRYSKLGLKVAIRVGMSRIKTKEEP IVLDTGTDAHIIVGTYEGIDYLLRAGKKIGNVGTVVIDEIHMLDDEERGAR LDGLIARLRKLYSNAQFIGLSATVGNPQELARKLGMKLVLYDERPVDLERH LIIARNESEKWRYIAKLCKAEAMRKSEKGFKGQTIVFTFSRRRCHELASFL TGQGLKAKAYHSGLPYVQRKLTEMEFQAQMIDVVVTTAALGAGVDFPASQV IFESLAMGNKWIŢVREFHQMLGRAGRPQYHEKGKVYIIVEPGKKYSAQMEG TEDEVALKLLTSPIEPVIVEWSDEFEEDNVLAHACVFNRLKVIEEVQSLCL GANQSAKNVLEKLMEKGLVKIYGDKVEATPYGRAVSMSFLLPREAEFIRDN LESTDPIEIAIKLLPFENVYLPGSLQREIESAVRGKISSNIFSSSFASVLE ELDKIIPEISPNAAERLFLIYQDFFNCPEQDCTEFAMERIGRKIIDLRREG YEPSKISEHFRKVYALILYPGDVFTWLDGIVRKLEAIERIARVFNKRRVVE DTIRVRREIEEGKILKGERR

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# FIG. 31

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MHKYFFPLPATKSTFLLPADLTTANPCFSKSLINSLSAWAPFLYIQCFSYL PLINFLNSLTYPLEMHILIKKAIKERFGKLNALQQLAFHKIRGEGKSVLII APTGSGKTEAAVIPILDAILRENLKPIAAIYIAPLKALNRDLLERLKWWEE KTGVIIEVRHGDTPTSKRLKQVKNPPHLLITTPEMLPAILTTKSFRPYLKN TKFIVIDEIGELIENKRGTQLILNLKRLELITEDKPIRIGLSATIGSEEKV RLWMEADEVVKPRLKKKYKFTVLYPQPIPEDEKLAEELKVPIEVATRLRVV WDIVEKHKKVLIFVNTRQFAEILGHRLKAWGKPVEVHHGSLSREARIEAEK KLKEGKIKALICTSSMELGIDIGDVDAVIQYMSPRQVNRLVQRAGRSKHRL WETSEAYIITTNVEDYLOSLAIAKLALEGKLEDVNPYENALDVLAHFIVGL TIEYRNVNITEPYSLAKSTYPYRKLSWEDYQKVLEILEEARIIRRDGDAIK LGKNAFKYYFENLSTIPDEISYAVIDIASGKSVGRLDENFVTELEESMEFI MHGRSWIVLEINEKERIIKVKESNNLESALPSWEGELIPVPLEVAEFVGKL KRELLWDKERALKLLEGVEFNKEELEVAISQLVESEPVASDRDIIIESYPK FVIIHADFGNKINEGLTRFISVFLSARYGNIFLPRSQAHGIIIRSPFRLNP EEIKEILLMKAEVGDIVARGIRDTPIYRWKMSAIAKRFGALRRDARIKKVE RLFEGTIIEKETFNEIYHDKIDIDKTEKILEKIRKGEIRMKTLFREEITPL SSSLATLGGEFLIRDILTQEEVEEIFREKLLDAELVMVCTNCGFSWRTKVR RVMDRVNELSCPKCDSKMIAPLHPKDSETFISALKKLKRGEKLSREEEKYY LRGLKAADLLKAYGKDALLALATYGVGVESATRILRDYRGKSLIKALIEAE KHYIOTRKFWE

# FIG. 32

VMLLRRDLIQPRIYQEVIYAKCKETNCLIVLPTGLGKTLIAMMIAEYRLTK
YGGKVLMLAPTKPLVLQHAESFRRLFNLPPEKIVALTGEKSPEERSKAWAR
AKVIVATPQTIENDLLAGRISLEDVSLIVFDEAHRAVGNYAYVFIAREYKR
QAKNPLVIGLTASPGSTPEKIMEVINNLGIEHIEYRSENSPDVRPYVKGIR
FEWVRVDLPEIYKEVRKLLREMLRDALKPLAETGLLESSSPDIPKKEVLRA
GQIINEEMAKGNHDLRGLLLYHAMALKLHHAIELLETQGLSALRAYIKKLY
EEAKAGSTKASKEIFSDKRMKKAISLLVQAKEIGLDHPKMDKLKEIIREQL
QRKQNSKIIVFTNYRETAKKIVNELVKDGIKAKRFVGQASKENDRGLSQRE
QKLILDEFARGEFNVLVATSVGEEGLDVPEVDLVVFYEPVPSAIRSIQRRG
RTGRHMPGRVIILMAKGTRDEAYYWSSRQKEKIMQETIAKVSQAIKKQKQT
SLVDFVREKESEKTSLDKWLKKEKEEATEKEEKKVKAQEGVKVVVDSRELR
SEVVKRLKLLGVKLEVKTLDVGDYIISEDVAIERKSANDFIQSIIDGRLFD
QVKRLKEAYSRPIMIVEGSLYGIRNVHPNAIRGAIAAVTVDFGVPIIFSST
PEETAQYIFLIAKREQEEREKPVRIRSEKKALTLAERQRLIVEGLPHVSAT
LARRLLKHFGSVERVFTASVAELMKVEGIGEKIAKEIRRVITAPYIEDEE

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# FIG. 33

LKGLFRDVILHNPHLFVYSYSDKGIIPFKHQFQTLYHAMLMRPVRLMIADE IGLGKTIQALLIAKYLDFRGEIEKALIVVPKVLREQWREEVKRILEEAPEV IENGSEIEWKLKRPRKYFIISIDLAKRYTEEILRQKWDLVIVDEVHNATLG TORYEFLKELTKNKDLNVIFLSATPHRGNNRDYLARLRLLDPTIPEEISPM HERKIYMKSRGTLVLRRTKKVVNELEGEVFKKCHFGAVVVEVSREEREFFE ELNRALFELIKDQADYSPLTLLAVIIRKRASSSYEAALKTLTRIVESAYIS GOERARGVESYIEKIFRMGYEELEIEEFNEIDDAIHKIIDEYRGFLTEEOL ERLRRVLELGKKIGSKDSKLEVISDIVAYHIRNGEKVIIFTEFRDTLEYVL **ERLPDILRRKHGIVLEKDDIAKLHGGMKSEEIEREINKFHERANLLVSTDV** ASEGLNLHVASVVINYEAPWSPIKLEQRVGRIWRLNQTRETKAYTIFLATE TDLDVLNNLYRKIMNIKEAVGSGPIIGRPIFEGDFENLWNEGAEEENREVS EYELILASIKGELKGYAGALVRTLRILKQKVEGAVPVNPAGSIRRELEIIL EDTPDVEVLKKIVNRNVPNPFRLVRGLLREAEGIEGIRVLVKGYDGSMDVY YAIFYDEDGREIYRYPILAENGKYLVGFNLLKRISEVLSKEYKVVRGASEE VDYKVKTLVMDNIYNLIVKKYLEYDSLNIKEGKIFKRLKVEIKKALEVKGI SEEEFEVIKRVPPEIMEVLGLDSTKIELPTNEYLKIFERNFVPLDKILESE KKAMEIVMELEKSRGYNVEDVSLREHYDIRAFTDGEEKYIEVKGHYPMLLL AELTEKEFEFAQKNEDKYWIYIVSNIAKDPVIVKIYKPFSQDRRVFVVKNG EDVEVNINIEIKKKDRHLLKLS

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### FIG. 34

VITLELHPSEIARYFELEECSHYFSNLLLRKRGELQEFEPIIRRKEIETIE LAKWGDEFELSLLQEFKKGEALKKLGVKELPRFYGFLTENDTPVRKFFEKY FKDGIIVEEDPDKLLEIINSEKSAVIYQAPLKGRIGKFDVSGRADFIIKVG KTLYLLEAKFTKEEKFYHRIQAIIYAHLLSQMIEGYEIKLAVVTKENFPIP SNFLRFPGDVEELKITLEEKLGGILREQELWIDARCTTCPFEALCLSKALE ERSLGLLSLPPGIIRILKEEGIKDLKDMAKLFEFKENSPTNFEEPSIKDPK KTOEIAKRTGINLLKLSRIAQAILKYLDEGETTPLFIPRTGYNLPMDERVG DVEPSYYPPRSLVKVFFYVQTSPITDTIIGISALVKNRQNGERIIVKFVDE PPIEVSDAQEKERMLLIEFFRDVIDAVKSLSPTDKVYLHMYFYNRKQRDDL MDAVKRHKEIRENNAVMALLSLRRAIDWESFSIIKDEIIRRHALPLSPGLG **FVTVATQFGYRWRRNKTFARMLEVVARRENGKINLKTLLNISETGIGPEYY** PIIDRDNEGIPFTLFWSALVKLATEEDNSRIKRDIRDILSQMVEALKTIEE RIPEOYKDAFVKKEGIPKEDLENFDIKKEELADILLEYLOLEFDARFRERS EYYRLPLSIRAYSEESALIKIENIEKKKNDCLLFGKIVLIDENGRIKEYNP KEVLIDIDEGSLVVVTPKKFLDKLRRDPVQRISKSPLGIVEAIDHETGKVV IRLIRVSPGRFTLKHSKFSCKNGLLTITYPEGEVKVTPGEIVIVDPSVDDI GMERAYNVLSEISQGELKHEIYQKVKAIYEGNTESRYEVNIWKKKHIEEFL SRVKKINEEQKKFAIDINNFLVTLQGPPGTGKTSGAIAPAILARAYSMVKD KKNGLFVVTGVSHRAVNEALIKTLKLKKELENTLKELRKIDLIRAVSGEEA IKIIKEELEREIKDDVDRIRFTAQEITHSSKQRSLDKYFANSGTVRIVFGT POTLNKLMKNTKEVELVVIDEASMMDLPMFFLSTKVCKGQVLLVGDHRQME PIOVHEWQLEDRKTFEEHYPFLSALNFIRFLRGELDERELKKFKRILGREP PEWKKDKNEVLPLYRLVRTYRLPQEIADLLSDAIYRADGIKLISEKKKRRK IIARHKDEFLSIVLDDRYPFVLILHDEGNSTKINELEAKIVEKIIKRVENI DIGVVVPYRAQKRLIASLIDSAQVDTVERFQGGEKSLIVISMTSSDPRIPG KGF

# FIG. 35

MNIKSFINRLKELVEIEREAEIEAMRLEMKRLSGVERERLGRAILSLNGKI VGEELGYFLVKYGRNKEIKTEISVGDLVVISKRDPLKSDLLGTVVEKGKRF IVVALEPVPEWALRDVRIDLYANDITFKRWIENLDRVRKAGKKALEFYLGL DEPSQGEEVSFEPFDKSLNPSQRKAIAKALGSEDFFLIHGPFGTGKTRTLV ELIRQEVKRGNKVLATAESNVAVDNLVERLAKDGVKIVRVGHPSRVSRHLH ETTLAYLITQHELYGELRELRVIGQSLAEKRDTYTKPTPKFRRGLSDAEII KLAEKGRGARGLSARLIKEMAEWIKLNRQVQKAFEDARKLEERIARDIIRE ADVVLTTNSSAALDVVDATDYDVAIIDEATQATIPSILIPLNKVDRFILAG DHKQLPPTILSLEAQELSHTLFEGLIEKYPWKSEMLTIQYRMNERIMEFPS REFYDGRIVADESVKNITLADLGIKVNASGIWRDILDPNNVLVFIDTCMLE NRFERQRRGSESRENPLEAKIVSKIVEKLLESGVKAEMMGVITPYDDQRDL ISLNVPEEVEVKTVDGYQGREKEVIILSFVRSNKAGEIGFLKDLRRLNVSL TRAKRKLIMIGDSSTLSSHETYRRLIEHVREKGLYVVLTKDSI

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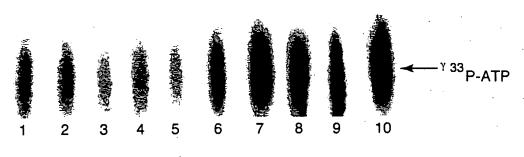


FIG. 36

#### ATPase ASSAY FROM IPTG INDUCED HELICASES



Title: Pfu REPLICATION ACCESSORY FACTORS AND METHODS OF USE
Inventors: Holly H. Hogrefe et al.
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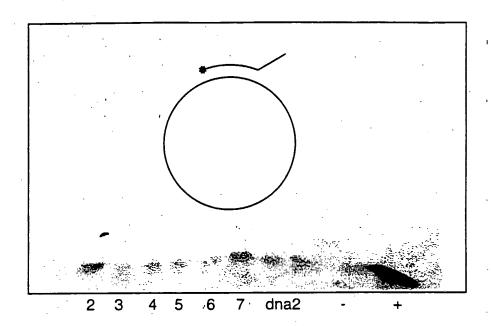


FIG. 38A

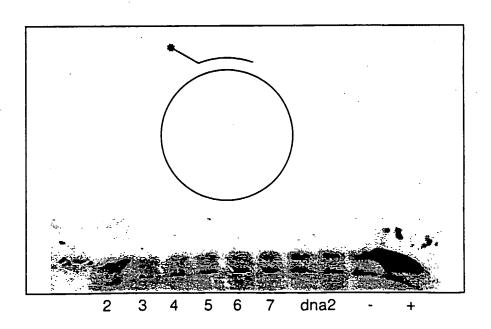


FIG. 38B

Title: Pfu REPLICATION ACCESSORY FACTORS AND METHODS OF USE Inventors: Holly H. Hogrefe et al. Application No.: Not Yet Assigned Filed: April 20, 2004 Attorney Docket No.: 04121.0161-02000 Page 34 of 37 (Figure 39)

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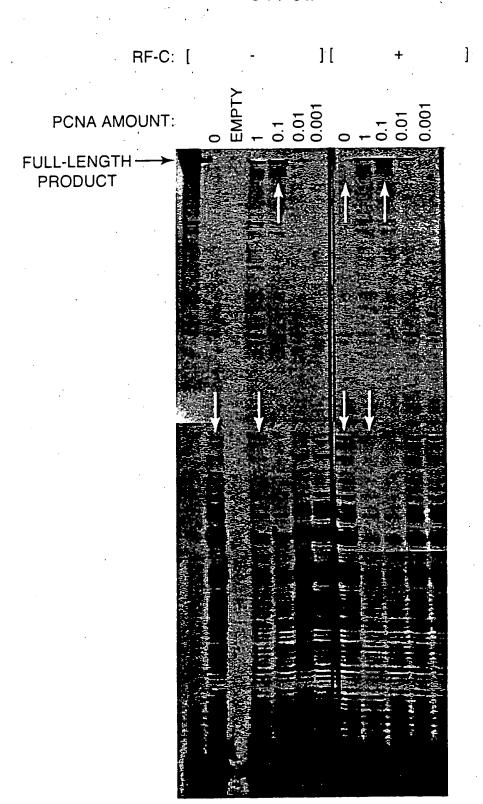


FIG. 39

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# FIG. 40

ATGAGGGTTGATGAGCTGAGAGTTGATGAGAGGATAAAGAGTACTTTGAAG GAGAGAGGTATCGAATCCTTTTACCCTCCCCAAGCCGAGGCCTTAAAGAGC GGGATATTGGAAGGTAAGAATGCATTAATTTCAATTCCAACGGCCAGCGGA AAAACACTAATTGCTGAGATTGCCATGGTTCATAGGATTTTGACCCAGGGA GGAAAGGCTGTATACATAGTCCCGCTGAAGGCCTTGGCTGAAGAAAAGTTT CAGGAGTTCCAGGATTGGGAGAAGATTGGGTTAAGAGTAGCGATGGCCACT GGGGATTACGACTCAAAGGATGAGTGGTTGGGGAAATACGACATAATCATT GCGACGGCTGAGAAGTTTGATTCCCTTTTAAGGCATGGCTCAAGTTGGATT AAGGATGTGAAGATTTTAGTTGCTGACGAGATTCATTTGATTGGTTCAAGA GACAGAGGAGCTACGCTTGAAGTTATCCTAGCTCATATGCTCGGAAAGGCC CAAATAATTGGACTCTCTGCAACGATAGGAAATCCAGAGGAGCTTGCGGAG TGGTTAAATGCCGAGCTAATAGTCAGTGACTGGAGGCCCGTTAAGCTTAGA AGGGGAGTTTTTTACCAAGGCTTTGTTACCTGGGAAGATGGAAGTATAGAC AGGTTTTCCTCCTGGGAAGAGTTAGTTTACGATGCAATTAGGAAGAAGAAA GGAGCGCTAATTTTTGTAAACATGAGAAGGAAGGCTGAGAGAGTAGCTTTG GAGCTTTCTAAAAAAGTTAAGTCTCTCCTCACGAAACCTGAGATTAGAGCT TTAAATGAATTGGCTGATTCCCTCGAGGAAAATCCCACAAATGAAAAGCTA GCTAAGGCCATTAGGGGTGGAGTTGCGTTCCACCACGCTGGTCTTGGGAGA GATGAGAGGGTTCTCGTGGAGGAGAACTTTAGAAAGGGTATAATAAAGGCC GTAGTTGCCACCCCAACACTTTCGGCGGGAATTAACACTCCAGCGTTTAGG GTGATTATAAGGGATATTTGGAGGTACTCTGACTTTGGAATGGAGAGAATT CCGATAATCGAGGTTCACCAAATGCTTGGGAGAGCTGGAAGGCCGAAGTAT GATGAGGTTGGGGAGGGAATAATAGTTTCTACAAGCGATGATCCGAGAGAG GTAATGAATCACTACATATTTGGAAAGCCTGAAAAACTGTTCTCCCAGCTC TCCAACGAGAGTAATTTGAGAAGTCAAGTTTTGGCCCTAATAGCGACCTTT GGCTATTCAACTGTGGAGGAGATTTTGAAGTTCATCTCAAACACATTCTAT GCTTATCAAAGGAAGGACACATACTCTTTAGAGGAGAAGATAAGGAACATA CTCTACTTCCTCCTAGAGAATGAGTTCATAGAGATATCCTTAGAGGATAAA ATAAGGCCGCTTTCCCTGGGAATTAGGACTGCAAAGCTTTATATCGATCCC TATACGGCCAAGATGTTCAAGGATAAAATGGAGGAAGTTGTTAAAGATCCA AATCCTATAGGAATATTTCACTTAATCTCCCTAACTCCGGATATAACCCCC TTCAACTACTCAAAGAGAGAATTTGAAAGGCTCGAAGAGGAATACTACGAA TTCAAGGATAGGTTATACTTTGACGATCCCTACATTTCGGGTTACGACCCC TACCTAGAGAGGAAGTTCTTCAGAGCTTTCAAAACTGCACTAGTGCTTCTG GCATGGATAAATGAAGTCCCTGAGGGAGAAATAGTTGAAAAGTACTCGGTG GAACCTGGGGACATCTATAGGATAGTTGAGACGGCTGAGTGGCTGGTGTAC TCTCTAAAGGAAATTGCAAAAGTTCTTGGAGCTTATGAGATCGTTGATTAT CTTGAAACATTGAGGGTTAGGGTCAAGTATGGGATTAGGGAGGAATTGATT CCCCTAATGCAACTCCCGTTGGTTGGAAGAAGGAGAGCTAGAGCTCTTTAC AATAGCGGATTTAGAAGTATAGAGGATATATCTCAAGCGAGGCCAGAAGAG CTTTTGAAAATCGAGGGGATAGGGGTCAAGACCGTTGAGGCTATCTTCAAG TTTCTTGGTAAGAATGTGAAAATTTCGGAGAAACCTAGAAAAAGTACCCTT GATTACTTTCTCAAATCTTGA

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# FIG. 41

MRVDELRVDERIKSTLKERGIESFYPPQAEALKSGILEGKNALISIPTASG
KTLIAEIAMVHRILTQGGKAVYIVPLKALAEEKFQEFQDWEKIGLRVAMAT
GDYDSKDEWLGKYDIIIATAEKFDSLLRHGSSWIKDVKILVADEIHLIGSR
DRGATLEVILAHMLGKAQIIGLSATIGNPEELAEWLNAELIVSDWRPVKLR
RGVFYQGFVTWEDGSIDRFSSWEELVYDAIRKKKGALIFVNMRRKAERVAL
ELSKKVKSLLTKPEIRALNELADSLEENPTNEKLAKAIRGGVAFHHAGLGR
DERVLVEENFRKGIIKAVVATPTLSAGINTPAFRVIIRDIWRYSDFGMERI
PIIEVHQMLGRAGRPKYDEVGEGIIVSTSDDPREVMNHYIFGKPEKLFSQL
SNESNLRSQVLALIATFGYSTVEEILKFISNTFYAYQRKDTYSLEEKIRNI
LYFLLENEFIEISLEDKIRPLSLGIRTAKLYIDPYTAKMFKDKMEEVVKDP
NPIGIFHLISLTPDITPFNYSKREFERLEEEYYEFKDRLYFDDPYISGYDP
YLERKFFRAFKTALVLLAWINEVPEGEIVEKYSVEPGDIYRIVETAEWLVY
SLKEIAKVLGAYEIVDYLETLRVRVKYGIREELIPLMQLPLVGRRRARALY
NSGFRSIEDISQARPEELLKIEGIGVKTVEAIFKFLGKNVKISEKPRKSTL
DYFLKS

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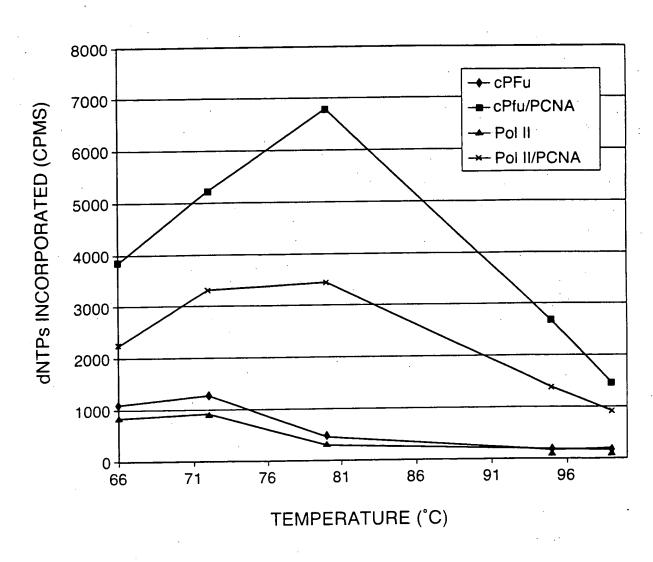


FIG. 42